

**What Is Claimed Is:**

1. A compound for activating the ubiquitination of a target protein comprising;
- a ubiquitination recognition element which is able to bind to either the E3 or E2 functional elements of the ubiquitination system, wherein said ubiquitination recognition element has a molecular weight less than 30,000 and has a binding affinity for said E3 and/or E2 elements of the ubiquitination system of at least  $10^2 \text{ M}^{-1}$  and;
  - a target protein binding element that is able to bind specifically to a target protein wherein said target protein binding element has a molecular weight of less than 30,000 and has a binding affinity for said target protein greater than  $10^5 \text{ M}^{-1}$ ,

wherein said ubiquitination recognition element is covalently linked to said target protein binding element

2. A compound for activating the ubiquitination of a target protein comprising;
- a ubiquitination recognition peptide element which is able to bind to either the E3 or E2 functional elements of the ubiquitination system, wherein said ubiquitination recognition peptide element has a molecular weight less than 30,000 and has a binding affinity for said E3 and/or E2 elements of the ubiquitination system of at least  $10^2 \text{ M}^{-1}$  and;
  - a target protein binding element that is able to bind specifically to a target protein wherein said target protein binding element has a molecular weight of less than 30,000 and has a binding affinity for said target protein greater than  $10^5 \text{ M}^{-1}$ ,

wherein said ubiquitination recognition peptide element is covalently linked to said target protein binding element.

wherein said ubiquitination recognition element is covalently linked to said target protein binding peptide element.

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5. A compound as in claim 1 wherein said ubiquitination recognition element has an affinity of at least  $10^3 \text{ M}^{-1}$  and a molecular weight between 50 and 10,000.
6. A compound as in claim 5 wherein said target protein binding element has a molecular weight from 50 to 10,000 and a binding affinity of greater than  $10^6 \text{ M}^{-1}$ .
7. A compound as in claim 1 wherein said ubiquitination recognition element has an affinity of at least  $10^4 \text{ M}^{-1}$  and a molecular weight between 50 and 3,000.
8. A compound as in claim 1 wherein said target protein binding element has a molecular weight from 50 to 3,000 and a binding affinity of greater than  $10^7 \text{ M}^{-1}$ .
9. A compound as in claim 5 wherein said target protein binding element has a molecular weight from 50 to 3,000 and a binding affinity of greater than  $10^8 \text{ M}^{-1}$ .
10. A compound as in claim 1 wherein said ubiquitination recognition element contains an amino acid with a free amino terminal selected from the group consisting of Phe, Arg, Lys, Trp, Leu, Asn, Asp, Gln, Tyr, His, Glu, Cys, Thr, Ser and Ala and oxidized derivatives thereof.
11. A compound as in claim 1 wherein said ubiquitination recognition element contains an amino acid selected from the group consisting of Phe, Arg, Lys, Asn, Asp, Gln, Glu and Cys.

12. A compound as in claim 1 wherein said ubiquitination recognition element contains an amino acid selected from the group consisting of Arg, Phe, Asp, Gln and Glu.
13. A compound as in claim 1 wherein said ubiquitination recognition element contains a moiety selected from the group consisting of Arg- $\epsilon$ Ahx-Cys, Arg- $\beta$ -Ala- $\epsilon$ Ahx-Cys, Arg- $\epsilon$ Ahx- $\epsilon$ Ahx-Cys, Phe- $\epsilon$ Ahx-Cys, Phe- $\beta$ -Ala- $\epsilon$ Ahx-Cys, Phe- $\epsilon$ Ahx- $\epsilon$ Ahx-Cys, Arg-Ala- $\epsilon$ Ahx-Cys, Arg-Ala- $\beta$ -Ala- $\epsilon$ Ahx-Cys, Arg-Ala- $\epsilon$ Ahx- $\epsilon$ Ahx-Cys, Phe-Ala- $\epsilon$ Ahx-Cys, Phe-Ala- $\beta$ -Ala- $\epsilon$ Ahx-Cys and Phe-Ala- $\epsilon$ Ahx- $\epsilon$ Ahx-Cys.
14. A compound as in claim 1 wherein said ubiquitination recognition element contains a moiety selected from the group consisting of; Arg- $\epsilon$ Ahx-Cys, Arg- $\beta$ -Ala- $\epsilon$ Ahx-Cys, Arg- $\epsilon$ Ahx- $\epsilon$ Ahx-Cys, Phe- $\epsilon$ Ahx-Cys, Phe- $\beta$ -Ala- $\epsilon$ Ahx-Cys, Phe- $\epsilon$ Ahx- $\epsilon$ Ahx-Cys.
15. A compound as in claim 1 wherein said recognition element contains a moiety selected from the group consisting of Phe- $\epsilon$ Ahx-Cys, Phe- $\beta$ -Ala- $\epsilon$ Ahx-Cys, Phe- $\epsilon$ Ahx- $\epsilon$ Ahx-Cys.
16. A compound as in claim 1 wherein said ubiquitination recognition element is a compound able to inhibit a ubiquitination reaction by binding to a recognition site of a ubiquitination system.
17. A compound as in claim 1 wherein said ubiquitination recognition element is a compound able to interact with the recognition site of the ubiquitination system, said recognition sites selected from the recognition sites for a



23. A compound as in claim 1 wherein said ubiquitination recognition element binds the same ubiquitination recognition site as an N-recognin or its equivalent.

24. A method of modulating the level and/or activity of at least one target protein in an eukaryotic cell via the modulation of ubiquitination of said at least one target protein comprising contacting said cell with a compound comprising;

- a) a ubiquitination recognition element which is able to bind to either the E3 or E2 elements of the ubiquitination system, wherein said ubiquitination recognition element has a molecular weight less than 30,000 and has a binding affinity for said E3 and/or E2 elements of the ubiquitination system of at least  $10^2 \text{ M}^{-1}$  and;
- b) a target protein binding element that is able to bind specifically to a target protein wherein said target protein binding element has a molecular weight of less than 30,000 and has a binding affinity for said target protein greater than  $10^5 \text{ M}^{-1}$ ,

wherein said ubiquitination recognition element is covalently linked to said target protein binding element.

25. The method of claim 24 where said at least one target protein is modulated to cause a physiological or metabolic change.

26. The method of claim 24 where said at least one target protein is modulated to cause a pharmacological change.

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27. The method of claim 24 where said at least one target protein is modulated to treat a disease.

28. The method of claim 24 where said contacting said cell is achieved by administering said compound to a mammal.

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29. The method of claim 28 where said at least one target protein is an antigen.

30. A method as in claim 29 wherein said mammal is a human.

31. A method of treating an infection in a mammal comprising administering to said mammal an amount of a compound sufficient to eliminate and/or reduce said infection said compound comprising;

- a) a ubiquitination recognition element which is able to bind to either the E3 or E2 elements of the ubiquitination system, wherein said ubiquitination recognition element has a molecular weight less than 30,000 and has a binding affinity for said E3 and/or E2 elements of the ubiquitination system of at least  $10^2 \text{ M}^{-1}$  and;
- b) a target protein binding element that is able to bind specifically to a target protein wherein said target protein binding element has a molecular weight of less than 30,000 and has a binding affinity for said target protein greater than  $10^5 \text{ M}^{-1}$ ,

wherein said ubiquitination recognition element is covalently linked to said target protein binding element.

32. The method of claim 31 wherein said infection is a viral infection.

33. The method of claim 31 wherein said infection is caused by a virus selected from the group consisting of hepatitis A, hepatitis B, hepatitis C, hepatitis G, HIV1, HIV2, Herpes, CMV, rabies, RSV.

34. The method of claim 31 wherein said infection is caused by a parasitic infection.

35. The method of claim 31 wherein said infection is caused by an eukaryotic organism.

SUB 36. A method of selectively targeting ubiquitination in a cell comprising contacting said cell with a compound as in claim 1.

37. The method of claim 36 where said ubiquitination recognition element is recognized by an E3 for the N-end rule.



38. A method of treating a tumor in a mammal comprising administering to said mammal an amount of a compound sufficient to reduce the size of said tumor, said compound comprising;

- a) a ubiquitination recognition element which is able to bind to either the E3 or E2 elements of the ubiquitination system, wherein said ubiquitination recognition element has a molecular weight less than 30,000 and has a binding affinity for said E3 and/or E2 elements of the ubiquitination system of at least  $10^2 \text{ M}^{-1}$  and;
- b) a target protein binding element that is able to bind specifically to a target protein wherein said target protein binding element has a molecular weight of less than 30,000 and has a binding affinity for said target protein greater than  $10^5 \text{ M}^{-1}$ ,

wherein said ubiquitination recognition element is covalently linked to said target protein binding element.

39. A method of generating a compound for activating ubiquitination of a target protein which comprises covalently linking a target protein binding element to a ubiquitination recognition element.

40. A method as in claim 24 wherein said compound activates the ubiquitination of a protein bound to said target protein.

41. A method for controlling pests, comprising administering to said pests an effective dose of the compound of claim 1.

42. A ubiquitination recognition element comprising at least one structural element selected from the group consisting of compound Z, Arg- $\epsilon$ Ahx-linker, Arg- $\beta$ -Ala- $\epsilon$ Ahx-linker, Arg- $\epsilon$ Ahx- $\epsilon$ Ahx-linker, Phe- $\epsilon$ Ahx-linker, Phe- $\beta$ -Ala- $\epsilon$ Ahx-linker, Phe- $\epsilon$ Ahx- $\epsilon$ Ahx-linker, Arg-Ala- $\epsilon$ Ahx-linker, Arg-Ala- $\beta$ -Ala- $\epsilon$ Ahx-linker, Arg-Ala- $\epsilon$ Ahx- $\epsilon$ Ahx-linker, Phe-Ala- $\epsilon$ Ahx-linker, Phe-Ala- $\beta$ -Ala- $\epsilon$ Ahx-linker, Phe-Ala- $\epsilon$ Ahx- $\epsilon$ Ahx-linker.

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